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Case report

The attempt of pregnancy modification in a case of fetal Ebstein's anomaly

Karolina Rydzewska[1], Julia Murlewska[2], Michał Krekora[3], Iwona Maroszyńska[4], Maciej Moll[5], Maria Respondek-Liberska[2,6]

[1]Medical student 6th grade, Student's Scientific Club of Prenatal Cardiology, Medical University of Lodz, Poland
[2]Department of Prenatal Cardiology, Polish Mother's Memorial Hospital Research Institute in Lodz, Poland
[3]Department of Obstetrics and Gynecology, Polish Mother's Memorial Hospital Research Institute in Lodz, Poland
[4]Department of Intensive Care and Congenital Malformations of Newborns and Infants, Polish Mother's Memorial Hospital Research Institute in Lodz, Poland
[5]Department of Cardiac Surgery, Polish Mothers' Memorial Hospital Research Institute in Lodz, Poland
[6]Department of Diagnoses and Prevention of Fetal Malformations, Polish Mother's Memorial Hospital Research Institute in Lodz, Poland

Abstract

Introduction: Ebstein's anomaly is a rare congenital heart defect (< 1% of all cases of congenital heart disease). Its distinctive feature is the displacement of the septal and posterior leaflets of the tricuspid valve towards the apex. The right atrium is enlarged, and the right ventricle is divided into two parts. The leaflets are often dysplastic. This leads to tricuspid regurgitation. Pulmonary stenosis or atresia is the most common associated defect. All these changes can lead, during the fetal life, to cardiomegaly, lung hypoplasia, heart failure of the fetus, or even intrauterine demise.

Case presentation: A 39-year-old G3P3 at 23 weeks of gestation had a detection of heart disease. She was admitted to our Institute for further management. The prenatal echocardiography exam showed the fetus with Ebstein's anomaly, pulmonary valve atresia, and cardiomegaly. Intrauterine digoxin and steroid treatment was started. Subsequent fetal echocardiographic monitoring was performed late in the third trimester. At 39 weeks of gestation the oxygen test was positive and oxygen therapy was ordered. Elective caesarean section was performed at 40 weeks of gestation, and a male newborn weighting 2860 g was delivered. On the 11th day of life, he underwent cardiac surgery in the same hospital and was discharged four weeks later in a good general condition.

Conclusion: Despite the fact that there are no recommendations for intrauterine therapy for fetal Ebstein's disease, this case shows the possibility of finding an alternative method of fetal treatment, which can be a combination of digoxin, steroids, and maternal oxygen therapy and early neonatal, handmade, tricuspid valve replacement.

Key words: digoxin, oxygen test, echocardiography monitoring.

Corresponding author:
Karolina Rydzewska
Students' Scientific Club of Prenatal Cardiology
Medical University of Lodz, Poland
e-mail: karolina.rydzewska@stud.umed.lodz.pl

Introduction

Ebstein's anomaly is a rare congenital heart disorder, occurring in 1 per 200,000 live births and accounting for < 1% of all cases of congenital heart disease [1–5]. However, in the fetal population this defect is more frequent and constitutes 3–7% of heart defects because in the majority of cases there is a short life span limited to prenatal and or neonatal life [6].

It arises from an aberration in myocardial development, which causes the characteristic abnormalities in the structure and function of the heart. The distinctive feature of the malformation is the displacement of the attachment points of the septal and posterior leaflets of the tricuspid valve towards the right ventricular apex. In this way, the right atrium is enlarged and the right ventricle is divided into two parts: the larger part is called the "atrialised ventricle", and the smaller one is the functional part of the ventricle. The leaflets are often dysplastic; the anterior leaflet is elongated and sail shaped. This leads to tricuspid regurgitation.

Additional associated anomalies include bicuspid or stenotic aortic valves, pulmonary atresia or hypoplastic pulmonary artery, subaortic stenosis, coarctation, mitral valve prolapse, accessory mitral valve tissue or muscle bands of the left ventricle, ventricular septal defects, and pulmonary stenosis [7]. All these changes can lead to cardiomegaly, lung hypoplasia, heart failure of the fetus, or even intrauterine demise.

Perinatal mortality (defined as fetal demise or death before neonatal discharge) remains high among fetuses diagnosed with Ebstein's anomaly; there are reports of up to 45% in recent large multicentre cohort series of fetuses with Ebstein's anomaly or tricuspid valve dysplasia, substantially higher than other forms of congenital heart disease in the current era [8, 9]. In the fetus, severe tricuspid regurgitation may lead to cardiomegaly, hydrops, and arrythmia, with demise rates as high as 48% [10]. Although neonatal mortality approached 80–90% in early series [4, 11–14], various single-centre series have reported reduced mortality in the past two decades, ranging from 17% to 56% [15–18].

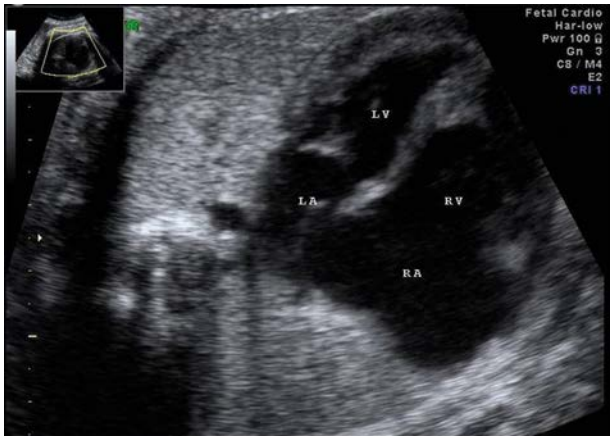

Figure 1. The first echocardiogram at 24 weeks of gestation, which confirmed Ebstein's anomaly. The four-chamber view – the asymmetric heart (right-sided chamber dilatation)

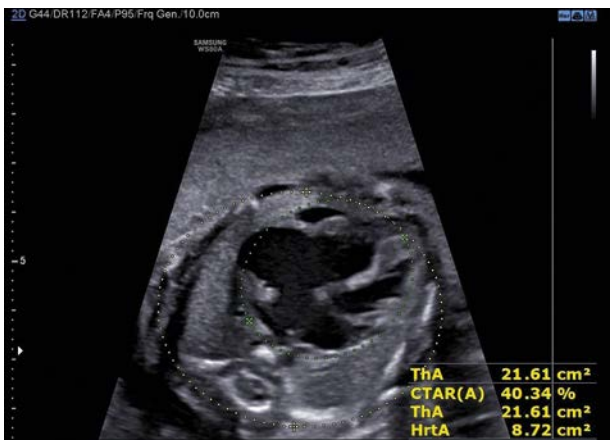

Figure 2. Fetal cardiomegaly – cardiac area to thoracic area ratio was 0.41

Case presentation

A 39-year-old multigravida, multipara, with no medical history, and no congenital disease in the family, had a routine obstetric ultrasound examination at 23 weeks of gestation. The fetal echocardiographic exam revealed an abnormal four-chamber view, although previous ultrasound exams did not show any abnormalities. The obstetrician suspected congenital heart defect and decided to refer the pregnant woman to the Polish Mother's Memorial Hospital Research Institute (Lodz, Poland), which is tertiary reference centre for prenatal cardiology.

At 24 weeks of gestation she was admitted to the Department of Prenatal Cardiology, which has extensive experience in diagnosing fetal malformations, especially congenital heart defects. The prenatal echocardiography exam showed the following: single fetus with Ebstein's anomaly, asymmetric heart (right side was significantly larger than the left side, huge right atrium) (Figure 1), cardiomegaly (heart area to thoracic area ratio was 0.41) (Figure 2), dysplastic tricuspid valve, tricuspid regurgitation (v max = 4.5 m/s), and pulmonary valve atresia (pulmonary valve flow was assessed with colour flow mapping). Despite the heart defect, the fetal measurements were appropriate for the gestational age. The fetal cardiovascular well-being was assessed by the Cardiovascular Profile Score (CVPS), and the result was 7 out of 10 points.

Due to the complexity of the heart defect, at 25 weeks of gestation intrauterine digoxin treatment was started. Furthermore, steroids were given to stimulate lung development (two doses of 12 mg betamethasone with an interval of 24 hours).

The digoxin treatment regimen was as follows: it was started 0.5 mg intravenously. After 12 hours, two doses of 0.5 mg intravenously with an interval of 12 hours. Afterward, the gravida was given 0.5 mg digoxin orally every 12 hours.

Unfortunately, the maternal response was not good – pregnant tachycardia occurred, although the tests (electrocardiogram, blood pressure, heart rate, serum electrolytes level) ordered before the start of therapy did not show any abnormalities. After seven days of therapy, due to an uncommon side effect (maternal tachycardia), it was decided to stop the administration of digoxin to the gravida. The second fetal echo-

cardiographic was done at 38 weeks of gestation. The fetus was too small for gestational age, and based on fetal echocardiography, the CVPS was 7 points. His heart area to thoracic area ratio was 0.41.

The next day an oxygen test was performed in order to evaluate fetal lung development. The test was positive; consequently, maternal hyperoxygenation therapy was started immediately after (and was continued until delivery) – 6 l/min oxygen was administered to the gravida using a face mask four times per day for 10 minutes for two weeks.

At 39 and 40 weeks of gestation, three more echo exams were done. The heart area to thoracic area ratio was 0.5. Fetal lung hypoplasia was considered. However, fetal cardiovascular well-being was rated at 8 points.

A full-term male neonate was born at 40 weeks of gestation by caesarean section due to the transverse position, with a birth weight of 2860 g and an Apgar score of 8. Prostaglandin E1 was administrated intravenously to the neonate with a dosage of 0.01 μg/kg/min (until cardiac surgery). From the first day of life, the newborn was breathing spontaneously (SaO_2 of 90%) despite cardiomegaly in chest X-ray (Figure 3). On the first day of life, echocardiogram confirmed the prenatal diagnosis of Ebstein's anomaly, severe tricuspid regurgitation, and pulmonary atresia.

On the 11th day of life, the newborn underwent cardiac surgery in the same hospital; tricuspid and pulmonary valves were reconstructed by a cardiac surgeon using special tissue called CorMatrix. After the surgery, a chest radiograph was performed, which showed improvement of cardiopulmonary parameters (Figure 4).

The newborn was discharged on the 27th day after the surgery in a good general condition.

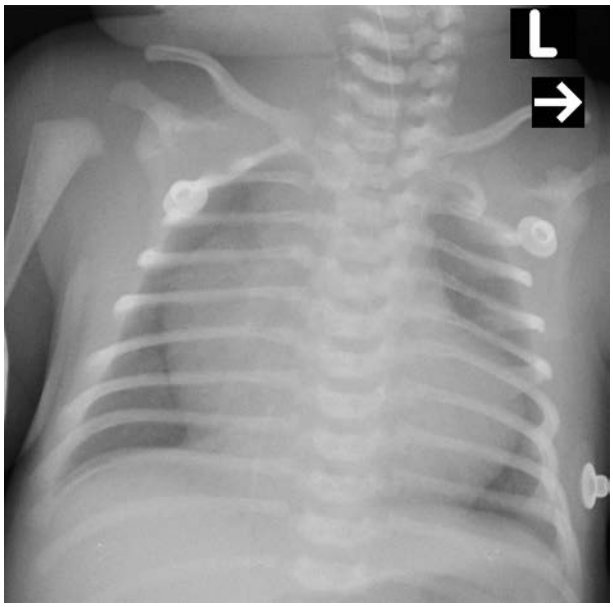

Figure 3. The first day of life. Chest radiograph shows significant cardiomegaly. Vascularity of the pulmonary fields is not visible

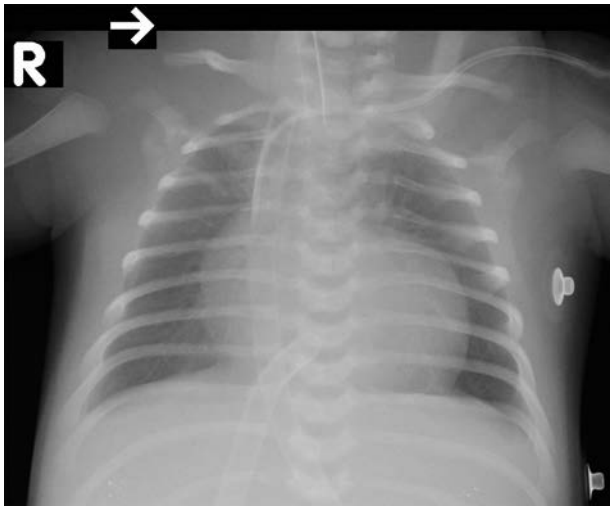

Figure 4. The first day after cardiac surgery (12th day of life). Chest radiograph shows an enlarged silhouette of the heart (however, the heart is significantly smaller than before the surgery); reduction in the transverse dimension of the heart; vascularity of the pulmonary fields is normal

Discussion

Ebstein's anomaly is a rare congenital heart defect. There is no recommendation for intrauterine treatment in Ebstein's anomaly. The diagnosis in the prenatal period carries a poor prognosis for both fetus and neonate [10]. In many centres in the world, pregnant women diagnosed with Ebstein's syndrome in the fetus choose the option of termination of pregnancy [19].

Prognosis is poor in the case of cardiomegaly, due to coexistence of lung hypoplasia [20]. The possible beneficial effects of transplacental digoxin therapy are discussed. The literature consists of a small number of cases showing an attempt to reduce the progression of cardiomegaly and improve the contractility of the heart in the case of fetal Ebstein's anomaly [20–23].

In the great majority of pregnant women, digoxin has no side effects on gravida, although an improvement of fetal haemodynamics is seen. The literature about intrauterine digoxin treatment is limited, and there are no reliable answers about the mechanism of the drug on the fetus.

Digoxin may be used for fetuses with congenital heart failure that might be due to a different pathogenic mechanism: ventricular diastolic overload (in the course of valvular incompetence), ventricular systolic overload (in the course of arterial pulmonary and systemic hypertension, aortic or pulmonary stenosis), or myocardial dysfunction due to myocarditis [24]. More research is needed in this complex issue.

Presently, in the Department of Prenatal Cardiology, the evaluation of pulmonary circulation is part of the echocardiographic examination - assessment of pulmonary vein flow to assess fetal lung development (between 18 and 22 weeks of gestation, as well as after 30 weeks of gestation). A functional assessment of pulmonary circulation – a hyperoxygenation test is additionally performed in the case of incorrect venous flows or other pathologies associated with the possibility of developing fetal lung hypoplasia. Abnormal lung development should be suspected when the test result is negative. The test result is a significant predictor of fetal survival. Survival probability of fetuses with positive test results was significantly higher than in the group with negative results [25, 26].

Materno-fetal hyperoxygenation in the third trimester results in fetal pulmonary vasodilation, increased venous return to the fetal heart, and improved hypoplastic fetal cardiovascular dimensions (significant increases in the dimensions of the mitral valve, ascending aorta, and aortic isthmus are observed). At the same time, assuming that not only the compression of the lungs but also the hypoxia of developing pulmonary alveoli contributes to the lung hypoplasia, it was assumed that perhaps hyperoxygenation therapy will contribute to the reduction of pulmonary resistance in the fetus. Adverse maternal, fetal, or neonatal events during and after chronic intermittent materno-fetal hyperoxygenation therapy were not observed during or after any of the treatment attempts. Given its simplicity, universal availability and potential benefits for large numbers of patients, intensive research in dedicated centres is now suggested [22, 27–30].

After birth, in cases of severe forms of Ebstein's anomaly, cardiac surgery is necessary: atrialised right ventricular plication and annuloplasty of right ventricular outflow tract [31].

In our case, the newborn has undergone early neonatal cardiac surgery. Tricuspid and pulmonary valves were reconstructed with special tissue called CorMatrix, due to the cardiac surgeon's decision. This is an acellular extracellular matrix that acts as a biological scaffold allowing for native integration of the valve and remodels into site-specific tissue. It has gathered increasing interest for its use in valve replacement because it eliminates the need for chronic anticoagulation therapy and reduces the risk of valve calcification and recurrent infection [32].

Conclusions

Despite the fact that there are no recommendations for intrauterine therapy for fetal Ebstein's disease, this case may show the possibility of finding an alternative method of predelivery fetal treatment, which can be the combination of digoxin, steroids, and maternal hyperoxygenation therapy and early neonatal cardiac surgery.

Conflict of interest

The authors declare no conflict of interest.

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Division of work:
Karolina Rydzewska (ORCID: 0000-0002-7220-4841): collection and/or assembly of data, data analysis and interpretation, writing the article
Julia Murlewska (ORCID: 0000-0002-8266-4585): critical revision of the article
Michał Krekora (ORCID: 0000-0002-5496-4556): critical revision of the article
Iwona Maroszyńska (ORCID: 0000-0003-4061-4843): critical revision of the article
Maciej Moll (ORCID: 0000-0002-2552-3436): critical revision of the article
Maria Respondek-Liberska (ORCID: 0000-0003-0238-2172): research concept and design, critical revision of the article, final approval of the article